NORTH CAROLINA STATE UNIVERSITY

INSTITUTIONAL REVIEW BOARD FOR THE USE OF HUMAN SUBJECTS IN RESEARCH

SUBMISSION FOR NEW STUDIES

Protocol Number 12229

Project Title

The GenX Exposure Study

IRB File Number:

Original Approval Date:

10/19/2017

Approval Period

10/19/2017 - 10/19/2018

Source of funding (if externally funded, enter PINS or RADAR number of funding proposal via 'Add New Sponsored Project Record' button below):

85701

NCSU Faculty point of contact for this protocol:NB: only this person has authority to submit the protocol

Hoppin, Jane A: Biological Sciences

Does any investigator associated with this project have a significant financial interest in, or other conflict of interest involving, the sponsor of this project? (Answer No if this project is not sponsored)

No

Is this conflict managed with a written management plan, and is the management plan being properly followed?

No

Preliminary Review Determination

Category:

Expedited Full Board

In lay language, provide a brief synopsis of the study (limit text to 1500 characters)

The purpose of this study is to assess exposure to GenX in people living in the Lower Cape Fear River Basin in response to community concerns and its relationship to clinical laboratory tests. We will measure GenX and other perfluoroalkyl substances (PFASs) in blood, urine and drinking water.

GenX is a chemical used in the production of Teflon, and it has been detected in the Cape Fear River, the drinking water source for Wilmington, NC. PFAS substances are used in the production of non-stick materials.

We plan to recruit 400 Wilmington area residents (100 women,100 men,100 boys and 100 girls) whose source of drinking water is the Cape Fear River. After administering a screener to determine eligibility, he/she will be asked to come to the local health department for biological sample collection and questionnaire administration. After the informed consent/assent document is reviewed and signed, participants will complete a brief questionnaire on their health, residential, and water use history and provide blood and urine samples. We will also measure the participant's height and weight and calculated body mass index. A member of the research team will come to the participant's home to collect a drinking water sample. We will analyze blood, urine, and drinking water for GenX and related chemicals. The blood and urine samples will also be used for clinical testing. All results from these tests will be provided to the participants. Samples will be stored for future use.

Briefly describe in lay language the purpose of the proposed research and why it is important.

GenX is a chemical generated in the production of non-stick coatings. This chemical has been detected in the Cape Fear River in North Carolina which serves as a drinking water source for ~300,000 residents in the Wilmington area. In June 2017, community concern about this chemical in drinking water resulted in public meetings of citizens trying to obtain information associated with consumption of this drinking water. As a result, the chemical plant (Chemours, formerly Dupont, in Fayetteville, NC) has stopped discharging GenX into the river. However, community concern still exists as this chemical has been discharged to the river since 1980.

Little is known about how GenX is stored in the body, the toxicity of GenX, or how long the chemical will remain in the environment. The results from the study will be shared with both the community as a whole and each individual

participant. We will have a Community Science Advisory Panel for the study to help advise about study protocols, methods of reporting back results to participants, and provide guidance on ongoing or new community concerns about GenX and other perfluorinated chemicals (PFAS). This class of chemicals poses a threat to the drinking water of >6 million Americans. This study will be among the first to have human data on GenX exposure.

This project is funded as part of the NIH Disaster Recovery Research program to respond to emerging environmental health threats. Residents in the Wilmington area are concerned about their drinking water. There have been community meetings, numerous facebook groups formed, and legislative activity related to GenX since June 2017. In July 2017, the governor denied Chemours discharge permit and the NC Department of Environmental Quality is now routinely sampling for GenX in the Cape Fear River. On August 31, 2017, the EPA identified new chemicals in the Cape Fear river that could be impacting drinking water quality. These chemicals called Nafion byproducts were released to the Cape Fear River until September 8, 2017. It is unclear when the discharge started. Here's a few links to the news coverage:
For example: https://www.cbsnews.com/news/wilmington-nc-cape-fear-river-water-tainted-genx-dupont-chemours/
http://portcitydaily.com/2017/08/31/epa-identifies-new-compounds-in-cape-fear-river-drinking-water-supply-nws/

The community is very concerned about these chemicals and whether they have been exposed. This study will be able to measure GenX as well as the Nafion byproducts present on the day of sampling.

My research qualifies for Exemption. Exempt research is minimal risk and must fit into the categories b.1 - b.6 found here: http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html

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Is this research being conducted by a student?

No

Is this research for a thesis?

No

Is this research for a dissertatiion?

No

Is this independent research?

No

Is this research for a course?

No

Do you currently intend to use the data for any purpose beyond the fulfillment of the class assignment?

No

Please explain

If so, please explain

If you anticipate additional NCSU-affiliated investigators (other than those listed on the Title tab) may be involved in this research, list them here indicating their name and department.

Detlef Knappe, MS, PhD
Professor, Department of Civil, Construction, and Environmental Engineering

Robert Smart, PhD
Director, Center for Human Health and the Environment

Katlyn May, MS
Director, Community Outreach and Engagement Core

Will the investigators be collaborating with researchers at any institutions or organizations outside of NC State?

Yes

List collaborating institutions and describe the nature of the collaboration

This is a very collaborative study with researchers at ECU and EPA as well as community partners of the Cape Fear River Watch and the New Hanover County Health Department.

Researchers at ECU will provide input into the study design, toxicology, and reporting back results to participants.

De-identified biological samples will be processed at ECU and stored at -80 until specimens are required. The clinical laboratory at Vidant at ECU will perform the clinical analyses. No identifying information will be stored at ECU. Co-investigators at ECU are Dr. David Collier, Associate Professor, Department of Pediatrics; Dr. Jamie DeWitt, Associate Professor of Toxicology and Pharmacology; and Dr. Suzanne Lea, Associate Professor of Epidemiology. Dr. Collier is a pediatrician and will facilitate the conduct of clinical analyses and interpretation of finding for individuals and their health care providers. He will be available to discuss adverse clinical findings, if necessary. Dr. DeWitt will provide toxicological expertise on GenX and will store de-identified biological samples. She will coordinate shipment of samples to EPA and the Vidant Clinical laboratories. Dr. Lea will provide public health expertise based on her experience as the North Carolina Public Health Association President. She will participate in field work activities related to subject recruitment and data collection. She will also identify ECU MPH students who would be interested in helping with data collection.

Drs. Andrew Lindstrom and Mark Strynar of US Environmental Protection Agency in RTP, NC. will oversee all of the chemcial analyses of GenX and related PFAS compounds with Dr. Strynar. They will receive de-identified samples for analysis. They will return sample results to Dr. Hoppin.

Our community partners Cape Fear River Watch and the New Hanover County Department of Health will facilitate the conduct of this research. Cape Fear River Watch is established in the Wilmington area and has many community connections including the president of the local NAACP on their board. They will be actively involved in the recruitment, screening, and consenting of study participants. They will receive IRB training before this occurs. They will also facilitate return of results to both individuals and the community. The New Hanover County Health Department will serve as the venue for sample collection. They have agreed to open their doors for weekend sample collection. They will also help in communicating about the study. We will subcontract phlebotemists for blood collection.

None of the outside investigators will receive PII. All samples will be labeled with the study ID only.

ECU's IRB will review following NC State IRB approval; they may request a reliance agreement. They will review for all relevant HIPAA concerns. We have included two HIPAA documents that their IRB requires; one for current use of samples and one for future use. EPA will seek similar approvals once NC State approval is complete.

What is NCSU's role in this research?

NCSU is responsible for the overall study design, hiring and supervising field staff, coordination of all collaborators, and operations for the conduct of the study, data analysis, and reporting results back to the community and individual participants. NC State will provide all human subjects training for study staff. All PII will be stored only at NC State following the completion of the field work.

Describe funding flow, if any (e.g. subcontractors)

This study will be supported by an R21 grant funded by the National Institute of Environmental Health Sciences, part of the National Institutes of Health, Department of Health and Human Services. Cape Fear River Watch will have a subcontract to perform screening, recruitment and community outreach for the duration of the project. NCSU will enter into a subcontract with a phlebotomy services firm to perform the blood draws for this study. We will also have a subcontract with the facilities management firm that manages the clinic offices for the New Hanover County Health Department. East Carolina University also has a subcontract for their role in the study.

Is this international research?

No

Identify the countries involved in this research

An IRB equivalent review for local and cultural context may be necessary for this study. Can you recommend consultants with cultural expertise who may be willing to provide this review?

Adults 18 - 64 in the general population?

Yes

NCSU students, faculty or staff?

No

Adults age 65 and older?

No

Minors (under age 18--be sure to include provision for parental consent and/or child assent)?

Yes

List ages or age range:

6-17

Could any of the children be "Wards of the State" (a child whose welfare is the responsibility of the state or other agency, institution, or entity)?

No

Please explain:

Prisoners (any individual involuntarily confined or detained in a penal institution -- can be detained pending arraignment, trial or sentencing)?

No

Pregnant women?

No

Are pregnant women the primary population or focus for this research?

No

Provide rationale for why they are the focus population and describe the risks associated with their involvment as participants

Fetuses?

No

Students?

No

Does the research involve normal educational practices?

No

Is the research being conducted in an accepted educational setting?

No

Are participants in a class taught by the principal investigator?

No

Are the research activities part of the required course requirements?

No

Will course credit be offered to participants?

No

Amount of credit?

No

If class credit will be given, list the amount and alternative ways to earn the same amount of credit.Note: the time it takes to gain the same amount of credit by the alternate means should be commensurate with the study task(s)

How will permission to conduct research be obtained from the school or district?

Will you utilize private academic records?

No

Explain the procedures and document permission for accessing these records.

Employees?

No

Describe where (in the workplace, out of the workplace) activities will be conducted.

From whom and how will permission to conduct research on the employees be obtained?

How will potential participants be approached and informed about the research so as to reduce any perceived coercion to participate?

Is the employer involved in the research activities in any way?

No

Please explain:

Will the employer receive any results from the research activities (i.e. reports, recommendations, etc.)?

No

Please explain. How will employee identities be protected in reports provided to employers?

Impaired decision making capacity/Legally incompetent?

No

How will competency be assessed and from whom will you obtain consent?

Mental/emotional/developmental/psychiatric challenges?

No

Identify the challenge and explain the unique risks for this population.

Describe any special provisions necessary for consent and other study activities (e.g., legal guardian for those unable to consent).

People with physical challenges?

No

Identify the challenge and explain the unique risks for this population.

Describe any special provisions necessary for working with this population (e.g., witnesses for the visually impaired).

Economically or educationally disadvantaged?

No

Racial, ethnic, religious and/or other minorities?

Yes

Non-English speakers?

No

Describe the procedures used to overcome any language barrier.

Will a translator be used?

No

Provide information about the translator (who they are, relation to the community, why you have selected them for use, confidentiality measures being utilized).

Explain the necessity for the use of the vulnerable populations listed.

This is a population based study which aims to characterize exposure to the entire population and therefore we need to include children and minorities.

State how, where, when, and by whom consent will be obtained from each participant group. Identify the type of consent (e.g., written, verbal, electronic, etc.). Label and submit all consent forms.

The informed consent process is an ongoing activity that begins with the first contact with a potential participant and continues during the course of the study. We will inform potential participants about the study in a variety of ways. We will have a number of Public Service Announcements by community leaders announcing the study. We will have flyers to hand out or to send via email. We will have a study website to inform people about the study.

People will be approached about the study in a number of venues. We are trying to recruit ~40% non-white minorities, so we will start our recruitment process in these communities. We will work with the head of the local NAACP, Deborah Maxwell, to help identify individuals who may be interested. We will also hold recruitment events at local public housing facilities and in a predominantly Hispanic area. Individuals will be informed about the study and will be given the opportunity to ask questions. They may be screened for the study at that time, or interested individuals can call the study's toll free number to get more information about the study. Individuals will either be screened in person or over the phone. All documents will be available in Spanish; these will be translated by UNC-W Spanish professor Amanda Boomershine. Dr. Boomershine will identify some of her students to help with translation during consent and field visits. Family members will not be expected to translate.

Participants who are eligible to participate will be asked to meet with a research staff member to review the written informed consent document, ask questions about the study, and if they agree, they will be asked to sign two copies of the document. The research team member obtaining consent will also sign the documents. A copy of the signed informed consent document will be given to the participants. For minors, parents will complete the screening questionnaire. If the minor child is eligible, we have separate assent forms for children (6-10 years and 11-17 years). The assent document will be read to and reviewed with the child in the presence of their parent; all questions will be answered and then the assent document signed by the child and the parental permission form signed by the parent. Assent and Permission copies will be provided to participants.

The Assent documents have been run through a readability calculator (http://www.readabilityformulas.com/freetests/six-readability-formulas.php). The assent form for 6-10 year olds was rated at Grade Level: 5
Reading Level: easy to read.
Reader's Age: 8-9 yrs. old (Fourth and Fifth graders)

The assent form for 11-17 year olds was rated at Grade Level: 7
Reading Level: fairly easy to read.
Reader's Age: 11-13 yrs. old (Sixth and Seventh graders)

If any participants are minors, describe the process for obtaining parental consent and minor's assent (minor's agreement to participate).

Children aged 6-10 will be given information verbally about the study by a research team member in the presence of their parent/legal guardian. If the child verbally agrees to participate, the parent/legal guardian will sign the parental permission form. A copy of the assent form and the script are attached.

For children aged 11-17, a research team member will review the written assent document in the presence of their parent/legal guardian. If the child agrees to participate, he/she will be asked to sign the assent document. Their parent/legal guardian will be asked to sign the parental permission form. The research team member obtaining assent/parental permission will also sign the documents. A copy of all signed documents will be given to the participant's parent/legal guardian.

Are you applying for a waiver of the requirement for consent (no consent information of any kind provided to participants) for any participant group(s) in your study?

No

Describe the procedures and/or participant group for which you are applying for a waiver, and justify why this waiver is needed and consent is not feasible.

Are you applying for an alteration (exclusion of one or more of the specific required elements) of consent for any participant group(s) in your study?

No

Identify which required elements of consent you are altering, describe the participant group(s) for which this waiver will apply, and justify why this waiver is needed.

Are you applying for a waiver of signed consent (consent information is provided, but participant signatures are not collected)? A waiver of signed consent may be granted only if: The research involves no more than minimal riskThe research involves no procedures for which consent is normally required outside of the research context.

No

Would a signed consent document be the only document or record linking the participant to the research?

No

Is there any deception of the human subjects involved in this study?

No

Describe why deception is necessary and describe the debriefing procedures.Does the deception require a waiver or alteration of informed consent information?Describe debriefing and/or disclosure procedures and submit materials for review.Are participants given the option to destroy their data if they do not want to be a part the study after disclosure?

For each participant group please indicate how many individuals from that group will be involved in the research. Estimates or ranges of the numbers

of participants are acceptable. Please be aware that participant numbers may affect study risk. If your participation totals differ by 10% from what was originally approved, notify the IRB.

100 adult males (ages 18+)
100 adult females (ages 18+)
100 boys (ages 6-17)
100 girls (ages 6-17)

How will potential participants be be found and selected for inclusion in the study?

The study team will work with community partners including the Cape Fear River Watch, Wilmington area NAACP leaders, UNC-Wilmington professors, and members of the New Hanover County Department of Health to help identify a representative sample of residents.

We will utilize Public Service Announcements, recruitment flyers and a study website to recruit potential participants. Our community partners will reach out to community members to inform them about the study. We will reach out to residents of public housing facilities, a local Hispanic community, as well as Cape Fear River Watch members and friends living in specific zip codes.

Individuals interested in the study will contact the study office using the toll free office to learn more and be screened for the study. We may also have some in person screening of potential participants. All in person screenings would happen in a private setting to ensure confidentiality.

All residents of New Hanover County ages 6 and older who are served by the Cape Fear Public Water Utility for at least the last 12 months will be eligible to participate. This exclusion criterion will allow us to know about an individual's potential exposure to GenX through drinking water. The Public Utility has both surface water (from the Cape Fear River and a potential source of GenX) and groundwater (less likely to contain GenX), so we will be able to assign potential exposure sources.

The remaining exclusion criteria relate to challenges for drawing blood. For this reason, we are excluding pregnant women and those who are HIV or Hepatitis C positive.

All study participants need to be willing to provide a blood and urine sample. If we are unable to collect these samples, they are still eligible to participate if they provided other information.

When individuals contact study staff by phone or in person about potentially participating, a staff member will administer the screener. Prior to enrollment in the study, we will only collect first names for contact information. Study staff will do screening on a computer, so that we can look up and confirm address information. The majority of screening will be done over the phone with study staff calling back individuals who have called to volunteer for the study; some screening may be done in person. Screening done in person will be done in a private area to ensure participant confidentiality.

We will use Qualtrics to implement our screener and have attached the screen shot from Qualtrics as well as the language for the screener. The data collected in Qualtrics will include only the responses to the questions regarding eligibility and will not include any identifying information. During the screening process we will look up the participant's address on a different screen; the address information will not be entered into the computer form. We will only save whether the address has municipal water or not.

The address lookup site is: https://cfpua.maps.arcgis.com/apps/webappviewer/index.html?id=2b8caaf8f458478aa488f7cf40587dd2
Interviewers will enter the address into the search box to confirm the address. The address is never entered onto the screening form.

We will save reasons for exclusion (live out of area, pregnant, HIV/Hep C positive), but we will not save any identifying information (address, phone number, DOB, name). For people who are eligible, we will obtain demographic information, so that we can ensure sufficient participation of non-white minorities. We will want to report in aggregate reasons for exclusion of the study. No IDs or linkage will be stored with the screener results; only Dr. Hoppin and selected study staff will have access to the aggregate file of screening. Once the screener is administered, the result is reported back

to the person doing the screener to establish eligibility; the data are stored on a secure Qualtrics server and are not accessible to field staff.

For people who are screened and found eligible, we will schedule an appointment for the clinic visit and a home visit for water collection.

For each participant group, how will potential participants be approached about the research and invited to participate? Please upload necessary scripts, templates, talking points, flyers, blurbs, and announcements.

Potential participants will receive a description of the study, the study office toll-free number and the study email to contact the study team at NCSU if interested in participating. NCSU's CHHE also hosts a GenX Exposure Study website.

We will approach people using a number of strategies. We will target non-white minorities through contact with the local NAACP and a Spanish professor involved in the Hispanic community. We will hold recruitment events on weekends where we will tell people about the study and invite them to participate. If they are interested we will screen at that time. Screening will happen in a private area. If they want to think about it, they can contact the study staff through phone or email to be screened. For a more broad based recruitment we will have local people doing Public Service Announcements about the study and these will have the study contact information. We will also send the flyer via email to residents of selected zip codes (based on water source) to invite them to participate. Finally, if we are having difficulty recruiting, we will use the outreach tools of the New Hanover County Health Department to invite people to participate via their facebook posts. We will use the flyer for this as well.

The research team will contact potential participants by phone to describe the study and the administer a brief screener to determine eligibility. If eligible, then the study staff member will schedule an appointment at the local health department for their enrollment visit.

We will also have trained staff in the community informing people about the study, screening them for eligibility and administering consent prior to their sample collection visit.

Describe any inclusion and exclusion criteria for your participants and describe why those criteria are necessary (If your study concentrates on a particular population, you do not need to repeat your description of that population here.)

Inclusion criteria: at least 12 months of consecutive residency (current) where the primary source of drinking water is from the Cape Fear Public Utility Authority; age 6 and older; and agree to complete all study activities at screening.

Exclusion criteria: less than 12 months of current residency in community area; well-supplied drinking water; HIV+ or HepC+ status; pregnant females; children under the age of 6; or does not agree to complete all study activities at screening.

Is there any relationship between researcher and participants - such as teacher/student; employer/employee?

No

What is the justification for using this participant group instead of an unrelated participant group? Please outline the steps taken to mitigate this relationship.

Describe any risks associated with conducting your research with a related participant group.

Describe how this relationship will be managed to reduce risk during the research.

How will risks to confidentiality be managed?

Address any concerns regarding data quality (e.g. non-candid responses) that could result from this relationship.

In the following questions describe in lay terms all study procedures that will be experienced by each group of participants in this study.For each group of participants in your study, provide a step-by-step description of what they will experience from beginning to end of the study activities.

Recruitment: Potential participants will be informed about the study at in-person at community meetings, via PSAs, the study website and/or by email. Interested community members will contact the study office either by phone or email. For those attending community meetings, they may be screened and consented in-person. For others, the research team

will call potential participants to screen for eligibility.

Screening: When individuals contact study staff by phone or in person about potentially participating, a staff member will administer the screener. Prior to enrollment in the study, we will only collect first names for contact information. Study staff will do screening on a computer, so that we can look up and confirm address information. After an individual is screened, the information will be destroyed at that time. We will save reasons for exclusion (live out of area, pregnant, HIV/Hep C positive), but we will not save any identifying information. We will want to report in aggregate reasons for exclusion of the study.

For people who are screened and found eligible, we will schedule an appointment for the clinic visit.

Consenting: If a person is eligible, and agrees to participate, he/she will be asked to meet with a research staff member in order to read, review, and sign two copies of the written informed consent/assent/parental permission form(s). A copy of all signed documents will be provided to them. Consenting may happen at the clinic visit, or may happen before the clinic visit with an in person visit with the participant to go over consent. This consent prior to clinic visit will speed the time in the clinic. All consenting will happen in a private area.

Questionnaire: Participants will be asked to complete a brief questionnaire, administered by research staff, with questions including, but not limited to, their health and residential history, and about their primary water source currently being used and primary water source used in the past. This questionnaire will be administered either before the clinic visit by study staff or during the clinic visit. Questionnaire will be administered after consent is received. Children will complete a shortened version of the Adult questionnaire. Children will not be asked about smoking, drinking, or pregnancy, or other sensitive topics. Parents will provide the residential history for the children.

Clinic Visit: Those who consent to participate will be asked to come to the New Hanover County Health Department Clinic. The Health clinic will be closed for their normal operations for our sample collection. At the clinic visit, a member of the research team will measure the participant's height and weight, a phlebotomist will collect 4 tubes of blood (about 3 Tablespoons - 40 mL), and the participant will provide a urine sample. For blood samples, we will collect 2 red top tubes for serum and 2 EDTA tubes for whole blood. For children under 11 years of age, we will collect 2 tubes of blood (less than 2 Tablespoons - 20 mL); these will both be serum tubes. We chose to administer an age cutoff, rather than a weight cutoff, as it was easier to implement as children 11 and older have a different assent form than children 6-10. The use of 11 years as a cut point will ensure that our participants weigh at least 50 pounds for collection of 4 tubes of blood (40 mL). 11 year old girls weigh on average 81.5 pounds and boys weigh 78.5 pounds. (https://www.disabled-world.com/artman/publish/height-weight-teens.shtml).

For urine samples, individuals will be given a urine collection cup labeled with their study ID and then directed to a private bathroom in the health department. Following sample collection, the participant will close the lid and either return the cup to study staff or leave it in the restroom if there is an appropriate location to do this that will ensure privacy. We will save approximately 30 mLs of urine from each person. The total time of this enrollment visit for will take approximately 30 - 45 minutes.

All biological samples (blood and urine) will be labelled with participant ID. All sample handling will happen in an area away from the study participants. Urine samples will be aliquoted into transport tubes (~30 mL). Red top tubes for serum will be spun in the same area and serum aliquoted into transfer tubes. One EDTA tube will be spun for plasma; the other will be kept as whole blood. Urine samples, serum and plasma transfer tubes and EDTA tubes will be refrigerated prior to shipment to ECU (Dr. DeWitt's lab) for storage. All samples will be shipped with a manifest and tracking information.

Drinking Water Sample Collection. Participants will also be asked to allow a study team member to collect a drinking water sample from their home (one per household if multiple family members are participating) in a container provided by the study. The field staff will come to their home, collect the water sample, identify the type of water filtration in the home (if any) and then leave. Field staff will then acidify the water sample with concentrated nitric acid or other

dechlorinating agent. The addition of acid will NOT happen in people's homes. This activity will take approximately 10-15 minutes. All water samples will be stored at room temperature. Water samples will be transferred to Dr. Knappe's lab for storage until the EPA laboratory is ready to analyze the samples.

After completion of study activities, participants will receive a thank you letter.

Reporting Back of Results: All materials used to report results back to participants will be approved by the IRB prior to use. Participants will be mailed the results from their urine analysis and the lipid panel, comprehensive metabolic panel, and thyroid function tests from the blood collection. Participants will also receive results of GenX and other chemical measurements in their urine, blood, and water samples. Participants will also be provided their height and weight measurements and their calculated Body Mass Index in this mailing. Participants can opt out of receiving any or all of these results. All results will be returned to study participants at the same time. When we return results to participants, we will remind them that these tests are not diagnostic and for research purposes only. However, we will provide them with the range of clinical norms for these tests and will encourage them to share them with their health care professional if they would like. If someone has values that are outside the normal range, we will discuss these findings first with Dr. Collier regarding their interpretation, and, if he feels that these results warrant a more timely contact, we will contact the IRB and get approval prior to contacting the participant with the results. There may be a delay between sample collection and sample analysis, as we plan to freeze all samples and deliver them as a batch to the clinical laboratory.

We will ask our Community Science Advisory Panel to help us in crafting appropriate messages about individual and community chemical exposures. All reporting back documents will be provided to the IRB for review and approval prior to use in the field.

Unused portions of samples will be stored for future analyses of chemicals or clinical measures. We will not store DNA.

Recontact: If chemicals are detected in blood and urine, we may recontact participants to ask for an additional blood and/or urine sample to better understand how these chemicals get removed from the body. People would be asked to provide 1 tube of blood (~1 Tablespoon) and/or an additional urine (3 Tablespoons) samples. If we choose to go this route, we will submit the materials to the IRB beforehand for review and approval.

Participants may be contacted in the future to complete other study activities. If a participant is contacted about follow-up study activities, they may refuse to participate. These documents will be submitted for approval by the IRB if we plan to recontact participants.

Describe how, where, when, and by whom data will be collected.

Screening: Potential participants will be screened over the phone or in-person for eligibility by study staff. All screening will happen in a private setting. No identifying data will be recorded from the screening process, just the reasons for exclusion.

Consent/Assent: Study staff will review and obtain written informed consent/assent/parental permission in a private setting. Parents will be present for all procedures with their children. Consent will either happen prior to the clinic visit or at the clinic visit. All consent/assent activities will happen in person. Individuals will receive a signed copy of their consent form. All consent forms will be stored in a locked file cabinet and office at NC State under Dr. Hoppin's supervision.

Questionnaire administration: Questionnaires will either be administered prior to the clinic visit or during the clinic visit by study staff. For each individual, we will collect their personally identifying information on a separate electronic questionnaire [PII Qx]. This questionnaire will be collected in a separate Qualtrics program so that the identifying information is not stored with the study questionnaire data. This questionnaire and all study materials will be labelled with the participant's ID number. For parents with participating children, the children's IDs will be linked to the parent who provided the residential history relevant to the child. Once the PII questionnaire is complete, we will administer the study questionnaire. We have separate questionnaires for adults and children, with the children's questionnaire much shorter than the adult questionnaire. Children will not be asked about smoking, drinking, pregnancy or other sensitive topics. The health questions focus on common outcomes (respiratory disease and symptoms, thyroid disease,

osteoporosis, etc); we have taken these from national studies such as NHANES. Because other PFAS chemicals have differential metabolism in males and females, we have included a few questions related to number of pregnancies and menopause as well. These main study questionnaires will be administered by study staff using a computer aided interview. We will use Qualtrics or similar program to create the questionnaire. Participants will be reminded that they can choose not to answer any question. The questionnaire should take <15 minutes. All questionnaire data will be stored on password protected computers and downloaded to a protected Google drive at least once per day, and before any breaks of study staff. Because we need address history to assign water use history, we will be collecting this in the main questionnaire. Once data collection is completed, we will geocode those addresses and remove this identifying information from the main data file.

Clinic visit. At the clinic visit (New Hanover County Health Department offices), we will measure height and weight, collect a blood sample and urine sample. Weight will be measured on a clinical scale and height will be measured using a stadiometer; both are standard anthropometric measurements. Height and weight will be recorded by study staff on a data sheet labelled with the participant's ID number. Each participant will have a data sheet that tracks the collection of height and weight, blood sample, and urine sample. This information will be entered into the computer following field work.

Blood samples will be collected by a contract phlebotomist trained in the collection of blood from children. We will draw four 10 mL tubes of blood (2 red tops for serum, 2 EDTA for whole blood and plasma) from individuals ages 11 and older; we will collect two 10 mL tubes (2 red top tubes for serum) of blood from children 6-10 years . All tubes will be labelled with participant's ID number. We will collect the serum sample tubes first as they are most important for our study. Participants will be informed about the risks of blood draw. The blood draw may involve a small risk of discomfort, bleeding or bruising, vein irritation, or infection, and a possibility of lightheadedness or fainting. All blood will be collected using sterile techniques. Site of blood draw will be bandaged. Participants will be instructed to contact the study toll free number if they have any problems at the site of the blood draw later. The two serum tubes (red tops) will be spun to separate serum. This will be done in a restricted area where participants are not present. All samples will be labelled with barcodes with the participant's ID. Samples will be stored refrigerated prior to shipment to ECU. No identifiers will travel with the samples.

The participants will be instructed on urine collection procedures. Individuals will be given a urine collection cup, labelled with their study ID and instructions about clean catch urine sample collection. A private restroom will be used for urine sample collection. After collection, participants will be asked to either return their cup to field staff or leave it on a table in the restroom. This will depend on whether study staff can retrieve a sample before the next person needs to use the restroom. Urine samples will be aliquoted to a smaller volume (30 mL ~ 3 Tablespoons) in a restricted laboratory area. All sample collection and transport containers will be labelled with subject ID. All urine samples will be refrigerated prior to shipment to ECU.

Study staff will schedule a water sample collection appointment at the participant's home. Water collection staff will have identifying information so that they know how to contact the study participant if they get lost or are running later. Participant identifying information will not be stored and will be destroyed after the collection of the sample. Study staff will collect the drinking water samples at the participant's home. Also during this visit, the study staff will determine the presence and type of water filtration in the home; this information will be recorded on a field collection form identified by study ID. Staff will run the tap for 1 minute, and then fill the water container. The container will be labelled with study ID. After leaving the participant's home, field staff will acidify the sample with concentrated nitric acid. This will not happen in people's homes. Water samples will be stored at room temperature prior to shipment to Dr. Knappe's lab at NC State.

Social?

Yes

Psychological?

No

Financial/Employability?

No

Legal?

No

Physical?

No

Academic?

No

Employment?

No

Financial?

No

Medical?

Yes

Private Behavior?

Yes

Economic Status?

No

Sexual Issues?

No

Religious Issues/Beliefs?

No

Describe the nature and degree of risk that this study poses. Describe the steps taken to minimize these risks. You CANNOT leave this blank, say 'N/A', none' or 'no risks'. You can say "There is minimal risk associated with this research."

There is minimal risk associated with this research.

Prior to enrollment, we are screening people for eligibility. We will first ask people their address to ensure that they live in the study region and then we will ask people whether they are HIV or Hepatitis C positive. We will ask these questions in a private area and will not collect or save this information; therefore, we will not have information on these outcomes for screened participants. If people are determined to be ineligible, we will only save the reason why so that we can describe it in the aggregate. All study staff involved in screening will be trained in human subjects protection and confidentiality issues. It is always possible that there would be a disclosure, but we will do everything we can to prevent that.

Blood collection. There are minor risks associated with blood collection. These are no different from a blood draw performed during routine medical appointments. The blood draw may involve a small risk of discomfort, bleeding or bruising, vein irritation, or infection, and a possibility of lightheadedness or fainting. We will use trained phlebotemists with pediatric experience to ensure the most comfortable experience for all participants. Participants will be instructed to contact the study office if they experience these symptoms at the blood collection site after they leave the clinic visit.

Urine collection. We will have a private restroom for urine collection. Individuals will be provided with a urine collection cup and instructions about clean catch urine samples. The cup will be labelled with the study ID. To ensure participant's privacy, we will collect the cup directly from the individual or, if there is a window between the lab and the restroom, we will instruct the participant to leave the sample there. The restroom will have a sink for the participant to wash their hands after sample collection.

Return of results. We recognize that individuals may be concerned about the results of the study, even though that's their motivation for participating. On the consent form, we give the participants the option not to receive their results if they so choose. Because of community concern about health effects due to GenX (even though there's no data on this chemical), we plan to return all results to individuals at the same time. While we anticipate that the clinical results will be available earlier than the GenX results, we do not want to panic people if they have something abnormal and have them attribute that to GenX when ultimately they may or may not have a high level. When we do return the clinical results, we will provide information for normal ranges for these tests to aid in the interpretation. If, by chance, we identify someone with an extreme value that needs to be addressed immediately, we will contact that person. Dr. Collier from ECU will aid in the interpretation of the clinical values. People will be advised that these are not diagnostic tests. We have as one of our community partners, the New Hanover County Health Department. If we need to refer an individual for some kind of

medical followup, they will be able to provide that information.
Because nothing is known about GenX and we do not know what we will find, we are assembling a community science advisory board to help in the interpretation of results. We will also provide information for local health care providers about the study and its findings, so that the medical community will be aware when patients come to them.

Questionnaire information. Our questionnaire will be administered in a private setting using a computer aided instrument. Participants will be told that they do not have to answer any question that they do not want to. We are collecting standard medical history questions, residential history, and water use information. All data will be protected on password protected computers and encrypted files. We will remove the identifying address information from the data files and only store the created variable water source at that address at that time.

Certificate of Confidentiality
Our study will have a Certificate of Confidentiality (CoC) issued by NIH. All grants funded October 1, 2017 or later will have a CoC issued automatically. It's part of the 21st Century Cures Act.

Relevant for my project, it protects: Studies where subjects may be involved in litigation related to exposures under study (e.g., breast implants, environmental or occupational exposures).

It provides an extra level of data protection. It protects against the release of PII for participants in research studies in legal settings.

Additionally I am meeting with NC State Office of General Counsel and Sponsored Programs to ensure that the data are protected to the extent possible under state and federal Freedom of Information Act requests.

If you are accessing private records, describe how you are gaining access to these records, what information you need from the records, and how you will receive/record data.

We are not accessing private records in this study.

Are you asking participants to disclose information about other individuals (e.g., friends, family, co-workers, etc.)?

No

You have indicated that you will ask participants to disclose information about other individuals (see Populations tab). Describe the data you will collect and discuss how you will protect confidentiality and the privacy of these third-party individuals.

If you are collecting information that participants might consider personal or sensitive or that if revealed might cause embarrassment, harm to reputation or could reasonably place the subjects at risk of criminal or civil liability, what measures will you take to protect participants from those risks?

We are screening participants for HIV and Hepatitis C status prior to enrollment. We are not collecting identifying information on individuals who are ineligible for the study, so we will not have this information.

If any of the study procedures could be considered risky in and of themselves (e.g. study procedures involving upsetting questions, stressful situations, physical risks, etc.) what measures will you take to protect participants from those risks?

We are using standard clinical protocols for the collection of blood, urine, and anthropometric measurements. There are minor risks associated with blood collection. These are no different from a blood draw performed during routine medical appointments. The blood draw may involve a small risk of discomfort, bleeding or bruising, vein irritation, or infection, and a possibility of lightheadedness or fainting. We will use trained phlebotemists with pediatric experience to ensure the most comfortable experience for all participants. Participants will be instructed to contact the study office if they experience these symptoms at the blood collection site after they leave the clinic visit.
Urine collection will be done in a private restroom, minimizing the risk of seeing someone else in the restroom. Sinks will be available for handwashing after collection.

Questionnaire information. Some individuals may feel uncomfortable answering questions about themselves.
Our questionnaire will be administered in a private setting using a computer aided instrument. Participants will be told that they do not have to answer any question that they do not want to. We are collecting standard medical history questions, residential history, and water use information. We have kept our questionnaire short and have minimized the questions that may be regarded as sensitive. Children are not asked sensitive questions. All data will be protected on password protected computers and encrypted files. We will remove the identifying address information from the data

files and only store the created variable water source at that address at that time.

Describe the anticipated direct benefits to be gained by each group of participants in this study (compensation is not a direct benefit).

Participants will receive results from GenX and other chemical measurements from their blood, urine and water samples collected. The following blood sample analyses: lipid panel; comprehensive metabolic panel; and thyroid function tests will also be provided to participants. They will also receive results from their urine analysis, height, weight and BMI measurements.

The research staff will mail a written report of these results. This report can be shared with their health care provider if they choose. If a minor child participates, the parent/legal guardian will be mailed those results. Participants may also choose not to receive the results of any of the clinical, height/weight/BMI and/or chemical measurements. Participants who opt out of receiving their results may change their mind at any time by contacting the Principal Investigator.

The other benefits are those to the community and society at large. The knowledge gained from this study will be of benefit to public health by identifying and describing potential health risks of exposure to GenX in drinking water.

If no direct benefit is expected for participants describe any indirect benefits that may be expected, such as to the scientific community or to society.

See above for direct benefits expected for participants, community and society at large.

Will you be receiving already existing data without identifiers for this study?

No

Will you be receiving already existing data which includes identifiers for this study?

No

Describe how the benefits balance out the risks of this study.

Will data be collected anonymously (meaning that you do not ever collect data in a way that would allow you to link any identifying information to a participant)?

No

Will any identifying information be recorded with the data (ex: name, phone number, IDs, e-mails, etc.)?

No

Will you use a master list, crosswalk, or other means of linking a participant's identity to the data?

Yes

Will it be possible to identify a participant indirectly from the data collected (i.e. indirect identification from demographic information)?

Yes

Audio recordings?

No

Video recordings?

No

Images?

No

Digital/electronic files?

Yes

Paper documents (including notes and journals)?

Yes

Physiological Responses?

No

Online survey?

No

Restricted Computer?

Yes

Password Protected files?

Yes

Firewall System?

Yes

Locked Private Office?

Yes

Locked Filing Cabinets?

Yes

Encrypted Files?

Yes

Describe all participant identifiers that will be collected (whether they will be retained or not) and explain why they are necessary.

Participant identifiers that will be collected include race/ethnicity, date of birth, residential history, and contact information including full name, phone, email, and physical address. These data will all be retained. These are all critical to the outcome measurements designed for this study. We need to retain all of this information in order to conduct this initial study as well as any potential future follow-up studies. We will also collect information about how to contact them via Facebook messenger; among some populations this is a useful way to recontact if phone numbers change.

We will store identifying information separately from the main data set. We will use date of birth to create an age variable that will be included in the analytical data set. For the residential history information, we will separate that from the main dataset, create geocodes and water history for those addresses, and then return the water history variable to the main dataset. Geocodes and addresses will be stored in a separate dataset.

This study will have a Certificate of Confidentiality through NIH. All grants funded October 1, 2017 or later will have a CoC issued automatically. It's part of the 21st Century Cures Act. It provides an extra level of data protection. It protects against the release of PII for participants in research studies in legal settings.

Additionally I am meeting with NC State Office of General Counsel and Sponsored Programs to ensure that the data are protected to the extent possible under state and federal Freedom of Information Act requests.

If any links between data and participants are to be retained, how will you protect the confidentiality of the data?

The personal identifiers will be kept in a linked file, not directly with the data sets. Date of birth will be converted to "age" in the data sets. Data sets and the linked file will be stored in password protected files with limited access within the NCSU system. Any paper records will be kept in locked file cabinets within locked, private offices at NCSU.

If you are collecting data electronically, what (if any) identifiable information will be collected by the host site (such as email and/or IP address) and will this information be reported to you?

We will have an NCSU hosted study email address that potential and actual participants may use to contact the NCSU study team. NCSU study staff will reply to emails either by email or phone. Email addresses will be stored with PII information in a secure environment.
The screener will be administered in Qualtrics, but no identifiable information will be recorded.

The questionnaire will be administered by NCSU study staff on NCSU issued tablets or laptop computers. The questionnaire will be programmed in Qualtrics. These data will be encrypted and downloaded into SAS or R data files.

Describe any ways that participants themselves or third parties discussed by participants could be identified indirectly from the data collected, and describe measures taken to protect identities.

A small risk exists in that other community members might notice a person is participating in the study since the enrollment visit is completed at a central, local facility. There will be separate, private stations to complete the study activities. Also, neighbors might notice a research staff member visiting a participant's home when the water sample is being collected.

Data will be stored securely in password protected files. No reference will be made in oral or written reports that could link an individual to the study. All participants will have a unique personal identification number used on the questionnaire, blood and urine specimens, and water samples, instead of names. In order to properly label questionnaires, specimens, and the water sample, certain research staff will have access to a list linking the study ID in both paper and digital form with personal identification information: name, date of birth, mailing and physical address, email, and telephone number(s). In addition, the NCSU Principal Investigator, Study Manager and NCSU field team members will have access to this information. The other investigators, laboratory staff, and data managers will not have access to the linked file.

To help us further protect participants' privacy, the study has obtained a Certificate of Confidentiality from the National Institutes of Health. The Certificate of Confidentiality helps to prevent the study team from being forced to give out

information that could identify participants, even by a court subpoena. However, the study team cannot guarantee that we will never have to give out information. The Certificate cannot be used to resist a demand for information by personnel from the United States Government, or other authorized people. Even in those cases, the NCSU study team will try to protect participant identify. The Certificate of Confidentiality does not prevent participants from voluntarily releasing information about themselves or their involvement in the study. With participant written permission, information can be provided to an insurer, employer, legal aide, or other person to whom they wish to release their information. There are no conditions under which the study team will voluntarily release participant information.

For all recordings of any type:Describe the type of recording(s) to be made Describe the safe storage of recordings Who will have access to the recordings? Will recordings be used in publications or data reporting? Will images be altered to de-identify?Will recordings be transcribed and by whom?

Not applicable

Describe how data will be reported (aggregate, individual responses, use of direct quotes) and describe how identities will be protected in study reports.

Data will be reported in aggregate form. No reports, oral or written, will allow an individual to be identified.

Will anyone besides the PI or the research team have access to the data (including completed surveys) from the moment they are collected until they are destroyed?

Possibly. Outside investigators may request de-identified data and samples collected in this study for other analyses. Requests will be made to Dr. Hoppin. If the proposed project is within the informed consent criteria, and no other investigators are researching that question, Dr. Hoppin may share samples. No identifiers will be shared without IRB approval.

Describe any compensation that participants will be eligible to receive, including what the compensation is, any eligibility requirements, and how it will be delivered.

There is no compensation for participating in this study.

Explain compensation provisions if the participant withdraws prior to completion of the study.

Not applicable.